UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,433	03/15/2005	Francois A. Auger	16867-2US MG/yl	2403

20988 7590 01/04/2006

OGILVY RENAULT LLP
1981 MCGILL COLLEGE AVENUE
SUITE 1600
MONTREAL, QC H3A2Y3
CANADA

EXAMINER	
FORD, ALLISON M	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 01/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/511,433	AUGER ET AL.	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *20 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *18-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☒ Claim(s) *1,3 and 9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 October 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 12/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 18-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 20 October 2005.

Drawings

The drawing submitted with the national stage application are objected to because there are two distinct figures shown, however, only one figure label ("Fig. 1"); additionally the specification only provides a brief description of a single figure, while there are two figures present. Additionally the drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: "a" and "b" and "c." Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

Claim 1 is objected to because of the following informalities: in the 4th line it appears the term "assembling" should be "assembly." Appropriate correction is required.

Claim 3 is objected to because of the following informalities: in the 1st line it appears "cell population" should read "cell populations" as two separate cell populations were previously referenced. Appropriate correction is required.

Claim 9 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Applicant's claim 9 requires the cell populations of claim 1 to comprise at least one cell type. However, any cell population would necessarily contain at least one cell type- as it consists of cells; rather, in order to further limit the method of claim 1, claim 9 would have to require the cell populations to comprise at least two types of cells.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's claim 1 is directed to a method for producing a continuous living tissue construct comprising allowing edge contact of at least two separate cell populations maintained in culture, each cell population forming a living tissue, for a period of time sufficient for assembly of said at least two cell populations into a single continuous living tissue construct. Applicant's claims 3 and 4 require the cell populations to be embedded into a collagen gel before being placed in culture for allowing edge contact.

In claims 1 and 16 the term "continuous living tissue construct" renders the claims indefinite, as it is not clear if applicants are claiming a tissue construct that lives forever, wherein 'continuous living' refers to a length of time the construct lives, or if applicants are referring to a spatial configuration of the tissue construct, wherein 'continuous' refers to the size or shape of the construct. If the later is true, wherein applicants intend to refer to a living tissue construct that is continuous in form or shape, it is unclear what dimension or parameter applicants are referring to, for example, it is not clear if applicants intend to refer to a living tissue construct which covers a continuous spans of space, or if the separate layers of a multilayered tissue construct are to be continuous with one another.

Additionally, in claims 1 and 3 the term "edge contact" renders the claims indefinite, as "edge contact" is not a common term in the art, and no explicit definition has been provided in the specification. While one of ordinary skill in the art recognizes that edge contact would refer to the different populations contacting at their edges, it is not clear if the cell populations are to be (i) butted against one another, side-by-side, so that perimeters of the cell populations are in contact, or (ii) layered one on top of another so that the top/bottom 'edges' of the cell populations are in contact. There is a significant structural difference in the two different 'edge contact' relationships, as the resulting products would be substantially distinct; therefore clarification is required.

In claims 3 and 4 it is unclear if the cell populations are to be embedded in a single gel, or if they are to be embedded in separate gels prior to being placed in culture to allow edge contact.

Claim 10 recites the limitation "said living tissue" in the first line of the claim. There is insufficient antecedent basis for this limitation in the claim. Parent claim 1 teaches both a 'continuous *living tissue* construct' and 'a *living tissue'* formed by each cell population; it is not clear which is being referenced.

In claims 13 and 14 it is unclear if the separator is a mechanical separator, so that the claim requires the cell populations to be separated from a tissue or organ prior to seeding, or if the separator is a

barrier or membrane which acts to separate the two cell populations from one another. In claim 15 it is clear the separator is a membrane or physical barrier between the two cell populations, however, such is not clear in claims 13 and 14. Additionally, in claims 13 and 14 (interpreting 'separator' to mean a physical barrier between the two cell populations) it appears the cell populations would not be capable of being in 'edge contact' or any type of contact with one another, as is required by parent claim 1, due to an impermeable separator. These claims appear to be omitting an essential step, the essential step being: removal of the separator between the at least two cell populations; or at least it would be necessary for the separator to at least be semi-permeable to allow some contact between the two cell populations.

Applicant's claim 15 requires the contact to be caused by removal of a separator between the at least two cell populations; however, no separator has been previously described as being placed between the two cell populations. While the actual term does lack antecedent basis in the claims, the step of removing a separator should be preceded by a step of placing a separator between the cell populations. Furthermore, it is not clear how, when, or why a separator is to be removed. The specification provides no guidance on how a separator, situated between two cell populations, would be removed from the graft without disrupting or destroying the cells adhered to the separator. Because the separator is removed before the living cell populations can develop into a single continuous tissue construct, it appears the separator is optional, as it is not required for the finished product, and in fact, must be removed before the construct can be formed. Applicant has not clearly defined the metes and bounds of the claimed method I so far as the separator is concerned.

In claim 16 the phrase "rolling the continuous living tissue construct" renders the claim indefinite, as it is not clear what is meant by "rolling." In the art of cell and tissue culture roller bottles are commonly used to "roll" cell cultures to maintain them in suspension; it is not clear if claims 16 and 17 intend to 'roll' the tissue construct in a roller bottle or other agitation-culture means, or if applicants

intend to 'roll' a planar tissue construct *around* a tube, bottle, jar, or some other cylindrical object, so as to create a tubular shape.

In claim 17 applicants claim the tubular tissue construct created by the method of claim 16 is a blood vessel; it is inappropriate to claim the tubular tissue construct *is* a blood vessel, as blood vessels are only truly created naturally within the body, rather it appears it would be more appropriate to claim the tubular tissue construct can *function as* a blood vessel, or is a *tissue engineered* blood vessel.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5-11 and 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by L'Heureux et al (FASEB, 1998).

Applicant's claim 1 is directed to a method for producing a continuous living tissue construct comprising allowing edge contact of at least two separate cell populations maintained in culture, each cell population forming a living tissue, for a period of time sufficient for assembly of said at least two cell populations into a single continuous living tissue construct. Claim 2 requires the cell populations to be partially or totally confluent. Claim 5 requires the cell populations to be composed of homologous or heterologous cells. Claim 6 requires the cell populations to be composed of mammalian cells. Claim 7 requires the cell populations to be composed of cells selected from the group consisting of mesenchymal cells, muscle cells, or fibroblasts. Claim 8 requires the muscle cells to be smooth muscle cells. Claim 9 requires the cell populations to comprise at least one cell type. Claim 10 requires the living tissue to be a sheet comprised of at least one cell type. Claim 11 requires the at least one of said cell populations is a

single cell layer, a tri-dimensional tissue construct, or a tissue graft. Claim 15 requires the contact to be caused by removal of a separator between the at least two cell populations, or by placing the cell populations in contact. Claim 16 is directed to a method for producing a tubular tissue construct comprising rolling the continuous tissue construct of claim 1. Claim 17 requires the tubular tissue construct to be a blood vessel.

L'Heureux et al teach a method for producing a tissue engineered blood vessel (which applicant calls a continuous living tissue construct), comprising separately culturing human vascular smooth muscle cells and human skin fibroblasts in standard tissue culture flasks to form sheets consisting of cells and extracellular matrix (ECM); the sheets of each cell type were removed from the culture flasks; then the VSMC sheet was first wrapped around an inert tubular support; the fibroblast sheet was then rolled around the VSMC sheet; and the graft was allowed to mature under standard culture conditions for approximately 8 weeks to allow formation of a tissue engineered blood vessel (which applicant calls a continuous living tissue construct) (See L'Heureux, Pg. 48, col. 2).

L'Heureux et al culture two distinct heterologous populations of cells into sheets, wherein the sheets consist of only cells and extracellular matrix proteins secreted by the cells; therefore each of these sheets of would be considered by one of ordinary skill in the art to be confluent cell layers (confluent also satisfies the limitation "partially confluent" as completely confluent cell cultures are also partially confluent) (Claims 2 and 10). The cell sheets each consist of a single cell layer, each cell sheet can be considered a tissue graft unto itself, and because cells are three-dimensional, the cell sheets can further be considered three-dimensional tissue grafts or three-dimensional tissue constructs (Claim 11). The two cell populations used to form the sheets are human vascular smooth muscle cells and human skin fibroblasts (both mammalian cell types); the cells within each population are homologous to the cells within that population, but are heterologous to the cells in the other population (Claims 5, 6, 8 and 9). Vascular smooth muscle cells are a type of mesenchymal cell (Claim 6). By wrapping the fibroblast sheet

around the smooth muscle cell sheet the faces of the cell populations are placed in contact with one another; contact of the faces of the cell populations is considered to be 'edge contact' (Claims 1 and 15). Additionally, because the cell populations (in sheet form) are rolled/wrapped around the tubular support, the tissue construct is considered to have been 'rolled' (Claim 16); the final product is a tissue engineered blood vessel (Claim 17). Therefore the reference anticipates the claimed subject matter.

Claims 1, 2, 5, 6, 9-11, and 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Quinn et al (US Patent 5,750,329).

Applicant's claim 1 is directed to a method for producing a continuous living tissue construct comprising allowing edge contact of at least two separate cell populations maintained in culture, each cell population forming a living tissue, for a period of time sufficient for assembly of said at least two cell populations into a single continuous living tissue construct. Claim 2 requires the cell populations to be partially or totally confluent. Claim 5 requires the cell populations to be composed of homologous or heterologous cells. Claim 6 requires the cell populations to be composed of mammalian cells. Claim 9 requires the cell populations to comprise at least one cell type. Claim 10 requires the living tissue to be a sheet comprised of at least one cell type. Claim 11 requires the at least one of said cell populations is a single cell layer, a tri-dimensional tissue construct, or a tissue graft. Claim 13 requires the at least one cell population to be separated by a separator. Claim 14 requires the separator to be an impermeable or allow selective passage of components contained in a culture medium. Claim 15 requires the contact to be caused by removal of a separator between the at least two cell populations, or by placing the cell populations in contact.

Quinn et al teach a process for forming an artificial organ system, specifically an artificial lung system, comprising placing an artificial microporous membrane (which applicant calls a separator) in a vessel so as to form an upper chamber and a lower chamber; then placing endothelial cells into the upper

chamber of the vessel under conditions such that the endothelial cells for a confluent cell layer on the upper side of the membrane; alveolar epithelial cells are then placed into the upper chamber under conditions such that the endothelial cells migrate through the membrane to form a confluent layer of endothelial cells on the lower side of the membrane and the alveolar epithelial cells form a confluent layer on the upper side of the membrane; then both cell populations are allowed to mature under appropriate culture conditions to form an artificial lung system consisting of two chambers, separated by a porous membrane, wherein alveolar epithelial cells form a confluent cell sheet on the upper side of the membrane, and endothelial cells form a confluent cell sheet on the lower side of the membrane (which applicant calls a continuous living tissue) (See Quinn et al, col. 8, ln 6-57). Quinn et al further teach an alternative process of forming the artificial lung system can be employed, which comprises first seeding endothelial cells on the upper side of the porous membrane so as to form a confluent cell layer on the membrane, then flipping the porous membrane over within the vessel, and seeding the alveolar epithelial cells on the other side of the membrane, so as to form a confluent cell layer on the other side of the membrane (See Quinn et al, col. 10, ln 63- col. 11, ln 12); in the alternative method it is not required for the endothelial cells to migrate through the membrane. Quinn et al teach mammalian cells, such as bovine or human cells can be used (See Quinn et al, col. 6, ln 7-38) (Claim 6).

Each of the confluent cell layers forms what applicant calls a living tissue sheet (Claim 2). The cell sheets are comprised of a single cell type, therefore the cells within each sheet are homologous to one another, but are heterologous to the cells in the other sheet (Claim 5). The sheets consist of a single cell layer, but due to the three-dimensional nature of cells, the living tissue sheets can also be described as tri-dimensional tissue constructs or tissue grafts (Claims 10 and 11). Quinn et al teach the porous membrane allows communication and interaction between the two different (heterologous) cell types, as would occur *in vivo*; because the membrane is porous the cell populations (which applicant calls living tissues) are considered in 'edge contact' with one another, thereby forming a continuous living tissue construct

(Claims 1 and 9). The cells are placed on either side of the membrane, therefore they are placed in contact with one another (Claim 15). Therefore the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al (US Patent 5,750,329).

Applicant's claims are directed to a method for producing a continuous living tissue construct comprising allowing edge contact of at least two separate cell populations maintained in culture, each cell population forming a living tissue, for a period of time sufficient for assembly of said at least two cell populations into a single continuous living tissue construct. Claim 3 require the cell populations to be embedded into a gel before being placed in culture for allowing edge contact. Claim 4 requires the gel to be a collagen gel.

Quinn et al teach a process for forming an artificial organ system, specifically an artificial lung system, comprising placing an artificial microporous membrane (which applicant calls a separator) in a vessel so as to form an upper chamber and a lower chamber; then placing endothelial cells into the upper chamber of the vessel under conditions such that the endothelial cells for a confluent cell layer on the upper side of the membrane; alveolar epithelial cells are then placed into the upper chamber under conditions such that the endothelial cells migrate through the membrane to form a confluent layer of endothelial cells on the lower side of the membrane and the alveolar epithelial cells form a confluent layer on the upper side of the membrane; then both cell populations are allowed to mature under appropriate

culture conditions to form an artificial lung system consisting of two chambers, separated by a porous membrane, wherein alveolar epithelial cells form a confluent cell sheet on the upper side of the membrane, and endothelial cells form a confluent cell sheet on the lower side of the membrane (which applicant calls a continuous living tissue) (See Quinn et al, col. 8, ln 6-57). Quinn et al further teach an alternative process of forming the artificial lung system can be employed, which comprises first seeding endothelial cells on the upper side of the porous membrane so as to form a confluent cell layer on the membrane, then flipping the porous membrane over within the vessel, and seeding the alveolar epithelial cells on the other side of the membrane, so as to form a confluent cell layer on the other side of the membrane (See Quinn et al, col. 10, ln 63- col. 11, ln 12); in the alternative method it is not required for the endothelial cells to migrate through the membrane.

Quinn et al further teach that a basement membrane material may additionally be coated on at least one side of the membrane so as to provide support for the seeded cells; particularly suitable basement membrane materials include collagen (See Quinn et al, col. 9, ln 1-20). Therefore, the epithelial cells can form a confluent layer on a collagen matrix on the membrane. Though Quinn et al does not teach first embedding the epithelial cells in a collagen gel matrix and then placing the cell-containing collagen gel in culture (on the membrane), it would have been well within the purview of one of ordinary skill in the art to first embed the cells in the collagen gel, and then place the gel on the membrane (in culture) (Claims 3 and 4). Culture of cells on collagen material is well known and accepted in the art; one of ordinary skill in the art would expect the same success culturing the cells whether the collagen was placed in culture first, and the cells subsequently added, or if the cells were placed on (which applicant calls embedded in) the collagen gel, and then the gel was placed in the culture. The order of such steps would be routinely optimized by one of ordinary skill in the art in practicing the invention based on experimental design choice. For example, in the alternative method of creating the artificial lung system (involving seeding the endothelial cells on one side of the membrane, then flipping the membrane over,

and finally seeding the epithelial cells on the other side of the membrane), one of ordinary skill in the art would be motivated to first combine the epithelial cells with the collagen gel (basement membrane material) and then to add the cell-containing collagen to the membrane in order to reduce the number of times the artificial lung system must be removed from incubation and exposed to the environment. By adding the collagen and epithelial cells in a single step the artificial lung system only needs to be manipulated once; however, if the collagen was to be added first, and then subsequently the epithelial cells were to be added, the artificial lung system would need to be handled twice. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over L'Heureux et al (FASEB, 1998) and/or Quinn et al (US Patent 5,750,329), each in view of Lanza et al (US Patent 6,808,704).

Applicant's claims are directed to a method for producing a continuous living tissue construct comprising allowing edge contact of at least two separate cell populations maintained in culture, each cell population forming a living tissue, for a period of time sufficient for assembly of said at least two cell populations into a single continuous living tissue construct. Claim 12 requires the at least one cell population to comprise genetically transformed cells.

L'Heureux et al teach a method for producing a tissue engineered blood vessel (which applicant calls a continuous living tissue construct), comprising separately culturing human vascular smooth muscle cells and human skin fibroblasts in standard tissue culture flasks to form sheets consisting of cells and extracellular matrix (ECM); the sheets of each cell type were removed from the culture flasks; then the VSMC sheet was first wrapped around an inert tubular support; the fibroblast sheet was then rolled around the VSMC sheet; and the graft was allowed to mature under standard culture conditions for

approximately 8 weeks to allow formation of a tissue engineered blood vessel (which applicant calls a continuous living tissue construct) (See L'Heureux, Pg. 48, col. 2).

Quinn et al teach a process for forming an artificial organ system, specifically an artificial lung system, comprising placing an artificial microporous membrane (which applicant calls a separator) in a vessel so as to form an upper chamber and a lower chamber; then placing endothelial cells into the upper chamber of the vessel under conditions such that the endothelial cells for a confluent cell layer on the upper side of the membrane; alveolar epithelial cells are then placed into the upper chamber under conditions such that the endothelial cells migrate through the membrane to form a confluent layer of endothelial cells on the lower side of the membrane and the alveolar epithelial cells form a confluent layer on the upper side of the membrane; then both cell populations are allowed to mature under appropriate culture conditions to form an artificial lung system consisting of two chambers, separated by a porous membrane, wherein alveolar epithelial cells form a confluent cell sheet on the upper side of the membrane, and endothelial cells form a confluent cell sheet on the lower side of the membrane (which applicant calls a continuous living tissue) (See Quinn et al, col. 8, ln 6-57).

Neither L'Heureux et al nor Quinn et al teach or suggest using genetically transformed cells as one of the cell populations used in their respective tissue constructs; however, at the time the invention was made, it would have been well within the purview of one of ordinary skill in the art to utilize genetically transformed cells in place of, or in addition to, the non-transformed mammalian cells described in the respective teachings, in the tissue constructs of L'Heureux et al and Quinn et al (Claim 13). In support, see Lanza et al; Lanza et al teach that when creating tissue constructs intended for implantation to regenerate or recover function of a damaged organ it can be beneficial to use genetically modified cells in creating the tissue construct (See Lanza et al, col. 8, ln 63-col. 9, ln 37). Lanza et al teach in cases where the patient's own organ has completely lost function, or when the cells are naturally deficient in a particular protein, one can harvest donor cells directly from the patient and transfect the autologous donor

cells with heterologous genes to compensate for the deficient proteins or functions, and then form an artificial tissue construct using the genetically modified cells (See Lanza et al, col. 9, ln 5-17). Alternatively, in cases where heterologous or xenogenic cells are to be used in the tissue construct (due to limited number of autologous or syngeneic donor cells), Lanza et al teach the heterologous or xenogenic cells can be genetically modified to knock-out genes that produce proteins known to illicit immune responses. Therefore, it would have been well within the purview of one of ordinary skill in the art to use appropriately genetically transformed cells in the methods of L'Heureux et al or Quinn et al. Particularly in the method of L'Heureux et al, wherein the tissue engineered blood vessel is to be implanted into a patient in need thereof, in cases where heterologous or xenogenic cells are to be used to form the tissue construct, it would be desirable to follow the teachings of Lanza et al and knock-out the genes known to be responsible for causing immune rejection responses in the patient. In the method of Quinn et al, one would be motivated to use genetically transformed cells in order to study the effect different protein expression levels had on drug effectiveness, as Quinn et al produce the artificial lung system to study test compounds. One of ordinary skill in the art would expect success using genetically transformed cells in the methods of L'Heureux et al and/or Quinn et al because methods are known for transforming cells (See Lanza et al), and one would have a reasonable expectation of successfully incorporating genetically modified cells in the tissue constructs. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Allison M Ford
Examiner
Art Unit 1651